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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/015,822	BAKER ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-35 and 38-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-35 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/2/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 02 February 2005 has been entered in full. Claims 28-35 are amended and claims 36-37 are cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 28-35 and 38-40 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objections to the specification at pg 2-3 of the previous Office Action (04 November 2004) are *withdrawn* in view of the amended specification and title (02 February 2005).

2. The rejection to claims 28-33, 36-37, and 39-40 under 35 U.S.C. 112, second paragraph, as set forth at pg 13-14 of the previous Office Action (04 November 2004) are *withdrawn* in view of the amended claims and cancelled claims (02 February 2005). Please see section on 35 U.S.C. 112, second paragraph below.

3. The rejection of claims 28-40 under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph (utility) as set forth at pg 3-8 of the previous Office Action (04 November 2004) is *withdrawn in part in* view of cancelled claims 36-37 (02 February 2005). Please see section on 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, below.

4. The rejections of claims 28-40 under 35 U.S.C. § 112, first paragraph (scope of enablement and written description) as set forth at pg 9-13 of the previous Office Action (04 November 2004) are *withdrawn in part* in view of cancelled claims 36-37 (02 February 2005).

Please see section on 35 U.S.C. § 112, first paragraph (scope of enablement and written description), below.

5. The supplemental information disclosure statement filed on 02 February 2005 has been considered.

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

6. Claims 28-35 and 38-40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation. The basis for this rejection is set forth for claims 28-40 at pg 3-8 of the previous Office Action (04 November 2004).

Specifically, claims 28-35 and 38-40 are directed to an isolated polypeptide having at least 80%, 85%, 90%, 95%, and 99% amino acid sequence identity to (a) the amino acid sequence of the polypeptide shown of SEQ ID NO: 374, (b) the amino acid sequence of the polypeptide of SEQ ID NO: 374, lacking its associated signal peptide, or (c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203465; wherein the nucleic acid encoding the polypeptide is amplified in lung or colon tumors. The claims also recite a chimeric polypeptide comprising a polypeptide fused to a heterologous polypeptide.

Applicant's arguments (02 February 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that the results presented in the instant specification have utility for the gene encoding the PRO1759 polypeptide. Applicant argues that the utilities of PRO1759

polypeptide include the use as a diagnostic tool, as well as therapeutically as a target for treatment, based on the data that PRO1759 cDNA is more highly expressed in lung tumor and colon tumor tissue compared to normal lung and colon tissue. Applicant states that the specification discloses that the nucleic acids encoding PRO1759 has a ΔCt value of >1.0, which is more than 2-fold increase, in at least 3 of the tumors listed in Table 8.

Applicant's arguments have been fully considered but are not found to be persuasive. In the instant case, the specification provides data showing a very small increase in DNA copy number in two different types of tumor tissue (lung and colon). However, there is no evidence regarding whether or not PRO1759 mRNA or polypeptide levels are also increased in these cancers. Furthermore, as discussed in the previous Office Action (04 November 2004), what is often seen is a *lack* of correlation between DNA amplification and increased peptide levels (Pennica, et al, Proc. Natl. Acad. Sci., 95: 14717-14722, 1998). As discussed by Haynes et al (1998, Electrophoresis, 19: 1862-1871), polypeptide levels cannot be accurately predicted from mRNA levels, and that, according to their results, the ratio varies from zero to 50-fold (page 1863). The literature cautions researchers against drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, Hu et al. (Journal of Proteome Research 2: 405-412, 2003) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (pg 408, middle of right column). Hu et al. discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant

correlation between expression level and a published role in the disease (see discussion section). Similarly, Chen et al. (2002, Molecular and Cellular Proteomics 1: 304-313) disclose that twenty-eight of the 165 protein blots (17%) or 21 of 98 genes (21.4%) had a statistically significant correlation between protein and mRNA expression (see Abstract and Table I). In addition, their results showed that no significant correlation between mRNA and protein expression was found (r= -0.025), if the average levels of mRNA or protein among all samples were applied across the 165 protein blots (98 genes). The reference also teaches that the mRNA/protein correlation coefficient varied among proteins with multiple isoforms, indicating potentially separate isoform-specific mechanisms for the regulation of protein abundance. In this study using a quantitative analysis of mRNA and protein expression within the same lung adenocarcinomas, it is showed that only a minority subset of the proteins exhibited a significant positive correlation with mRNA abundance.

Given the small increase in DNA copy number of PRO1759, and the evidence provided by the current literature, it is clear that one skilled in the art would not assume that a small increase in gene copy number would correlate with significantly increased mRNA or polypeptide levels. Further research needs to be done to determine whether the small increase in PRO1759 DNA supports a role for the peptide in the cancerous tissue; such a role has not been suggested by the instant disclosure. Such further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. As discussed in Brenner v. Manson, (1966, 383 U.S. 519, 148 USPQ 689), the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and,
>
> "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Accordingly, the specification's assertions that the PRO1759 polynucleotides encoding the claimed polypeptides have utility in the fields of cancer diagnostics and cancer therapeutics are not substantial.

Furthermore, the declaration of Dr. Goddard, filed under 37 CFR 1.132 (02 February 2005), is insufficient to overcome the rejection of claims 28-35 and 38-40, based upon 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph as set forth in the last Office Action (04 November 2004). Similarly, the declaration of Dr. Ashkenazi, filed under 37 CFR 1.132 (02 February 2005), is insufficient to overcome the rejection of claims 28-35 and 38-40, based upon 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph as set forth in the previous Office Action. Likewise, the declaration of Dr. Polakis, filed under 37 CFR 1.132 (02 February 2005), is insufficient to overcome the rejection of claims 28-35 and 38-40, based upon 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph as set forth in the last Office Action because:

Specifically, at page 11 of the response of 02 February 2005, Applicant discusses the accuracy of the Taq DNA polymerase assay, stating that the Taqman PCR technique is sensitive enough to detect at least a 2-fold increase in gene copy number (paragraph 1) and that this increase is significant and useful. Applicant directs the Examiner to page 3 of the Dr. Goddard

declaration that describes the gene amplification technique in the present application and references that attest to the use of this technique in diagnostic and prognostic fashion. This argument has been fully considered but is not deemed persuasive because it evinces that the instant specification provides a mere invitation to experiment, and not a readily available utility. The PRO1759 gene has *not* been associated with tumor formation or the development of cancer, nor has it been shown to be predictive of such. The specification merely demonstrates that the PRO1759 nucleic acid was amplified in two cancer samples, to a minor degree (about 2.5 fold). No mutation or translocation of PRO1759 has been associated with any type of cancer versus normal tissue. It is not known whether PRO1759 is expressed in corresponding normal tissues, and what the relative levels of expression are. In the absence of any of the above information, all that the specification does is present evidence that the DNA encoding PRO1759 is amplified in a variety of samples and invites the artisan to determine the significance of this increase. One cannot determine from the data in the specification whether the observed "amplification" of nucleic acid is due to increase in chromosomal copy number, or alternatively due to an increase in transcription rates. It remains that, as evidenced by Pennica et al., the issue is simply not predictable, and the specification presents a mere invitation to experiment.

Furthermore, the Declaration does not provide data such that the examiner can independently draw conclusions. Only Dr. Goddard's conclusions are provided in the declaration. It is noted that the literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, as discussed above, Hu et al. (2003, Journal of Proteome Research 2:405-412) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer

samples and normal samples in a microarray (pg 408, middle of right column) and discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section). The instant specification also does not demonstrate that the increased copy number of PRO1759 DNA in human lung tumors and colon tumors leads to an increased expression of PRO1759 polypeptide in these tumors. Therefore, since Applicants does not provide information regarding the level of expression, an activity, or a role in cancer or any other disease for the PRO1759 polypeptide, the polynucleotide and polypeptide lack a substantial utility or well established utility.

At page 12 of the response of 02 February 2005, Applicant asserts that the Examiner has not shown whether the lack or correlation observed for the family of WISP polypeptides (as cited in Pennica et al. by the examiner in the previous Office Action) is typical, or is merely a discrepancy an exception to the rule of correlation. The Office agrees with the Applicant in that the Pennica et al. reference does not discuss the relationship of level of mRNA and level of protein expression. However, this reference was cited by the Office to show the lack of correlation of between DNA amplification and gene expression. There is no evidence to support Applicant's assertion that there is working hypothesis, among those skilled in the art is that there is a direct correlation between gene levels and protein levels in cancer. In addition, even if there were a correlation between gene levels and protein levels, Applicant has not established a nexus between the DNA of instant invention and PRO1759 protein. Applicant also asserts that the data

in the Haynes et al. reference (also cited by the examiner in the previous Office Action) meets the "more likely than not standard" and shows that a positive correlation exists between mRNA and protein. However, Haynes et al, teaches that polypeptide levels cannot be accurately predicted from mRNA levels, and that, according to their results, the ratio varies from zero to 50-fold (page 1863). The literature cautions researchers against drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. This teaching is echoed in Chen et al (Molecular and Cellular Proteomics 1: 304-313, 2003). Specifically, Chen et al. disclose that twenty-eight of the 165 protein blots (17%) or 21 of 98 genes (21.4%) had a statistically significant correlation between protein and mRNA expression (see Abstract and Table I). In addition, their results showed that no significant correlation between mRNA and protein expression was found ($r = -0.025$), if the average levels of mRNA or protein among all samples were applied across the 165 protein blots (98 genes). The reference also teaches that the mRNA/protein correlation coefficient varied among proteins with multiple isoforms, indicating potentially separate isoform-specific mechanisms for the regulation of protein abundance. In this study using a quantitative analysis of mRNA and protein expression within the same lung adenocarcinomas, it is showed that only a minority subset of the proteins exhibited a significant positive correlation with mRNA abundance.

Applicant also contends that a polypeptide would have diagnostic utility even if there is no positive correlation between gene expression and expression of the encoded polypeptide. Further, it is asserted that even if there was no correlation between gene expression and increased or decreased protein expression for PRO1759, the gene that is over-expressed or under expressed in cancer would still have credible, specific and substantial utility. Applicant asserts that this

position is supported by the declaration filed under 37 CFR 1.132 (02 February 2005) by staff scientist Ashkenazi. It claims that the purpose of the experiments that measured increases in gene copy number was to identify tumor cell markers useful for cancer treatment (pages 1-2, declaration, 02 February 2005) and to identify cancers for which there was gene product over-expression (page 2). The Ashkenazi declaration further argues that, even when amplification of a gene in a tumor does not correlate with an increase in polypeptide expression, the absence of the gene product over-expression still provides significant information for cancer diagnosis and treatment. The examiner agrees that evidence regarding lack of over-expression would also be useful. However, there is no evidence as to whether the gene products (such as the PRO1759 polypeptide) are over-expressed or not. Further research is required to determine such. Thus, the asserted utility is not substantial. Applicant provides evidence in the form of a publication by Hanna et al. (Pathology Assoc Med Labratories August 1999, submitted 02 February 2005). Applicant contends that the publication teaches that the HER-2/neu gene is over-expressed in breast cancers, and teaches that diagnosis of breast cancer includes testing both the amplification of the HER-2/neu gene as well as over-expression of the HER-2/neu gene product. Applicant argues that the disclosed assay leads to a more accurate classification of the cancer and a more effective treatment of it. The examiner agrees. However, Hanna et al. supports the instant rejection, in that Hanna et al. show that gene amplification does not reliably correlate with polypeptide over-expression, and thus the level of polypeptide expression must be tested empirically.

Applicant also refers to three additional articles (Orntoft et al., Hyman et al., and Pollack et al. as providing evidence that gene amplification generally results in elevated levels of the

encoded polypeptide. Applicant characterizes Ornoft et al. as teaching in general (18 of 23 cases) chromosomal areas with more than 2-fold gain of DNA showed corresponding increase in mRNA transcripts. Applicant further characterizes Hyman et al. as providing evidence of a prominent global influence of copy number changes on gene expression levels. Applicant also states that Pollack et al. teach that 62% of highly amplified genes show moderately or highly elevated expression and that, on average, a 2-fold change in DNA copy number is associated with a 1.5-fold change in mRNA levels.

However, Ornoft et al. appear to have looked at increased DNA content over large regions of chromosomes and comparing that to mRNA and polypeptide levels from the chromosomal region. Their approach to investigating gene copy number was termed CGH. Ornoft et al. do not appear to look at gene amplification, mRNA levels and polypeptide levels from a single gene at a time. The instant specification reports data regarding amplification of individual gene, which may or may not be in a chromosomal region, which that is highly amplified. Ornoft et al. concentrated on regions of chromosomes with strong gains of chromosomal material containing clusters of genes (pg 40). This analysis was not done for PRO1759 in the instant specification. That is, it is not clear whether or not PRO1759 is in a gene cluster in a region of a chromosome that is highly amplified. Therefore, the relevance, if any of Ornoft et al. is not clear. Hyman et al. also used CGH approach in their research. Less than half (44%) of highly amplified genes showed over expression (abstract). Polypeptide levels were not investigated. Therefore, Hyman et al. also do not support utility of the polynucleotide encoding the polypeptides of the instant invention. Pollack et al., using CGH technology, concentrate on large chromosome regions showing high amplification (pg 12965). However, Pollack et al. did

not investigate or show a relationship with amplification and polypeptide expression. In fact, the authors caution that elevated expression of an amplified gene cannot alone be considered strong independent evidence of candidate oncogene's role in tumorigenesis (pg 12968). Thus, these references collectively do not teach, as Applicant contends, that there is a direct correlation between increased mRNA levels and increased levels of encoded protein. Accordingly, the Applicants' assertions that the polynucleotides encoding the PRO1759 polypeptides have utility in the cancer diagnostics are not substantial.

Although, Dr. Polakis states that it remains a central dogma in molecular biology that increased mRNA levels are predictive of corresponding increased levels of the encoded polypeptide, it is important to note that the instant specification provides no information regarding differential mRNA levels of PRO1759 in tumor samples as contrasted to normal tissue samples or the corresponding protein levels. Only gene amplification data were presented. Therefore, the declaration is insufficient to overcome the rejection of claims 28-35 and 38-40 based upon 35 U.S.C. § 101 and 112, first paragraph, since it is limited to a discussion of data regarding the correlation of mRNA levels and polypeptide levels. Furthermore, the declaration does not provide data such that the examiner can independently draw conclusions.

35 U.S.C. § 112, first paragraph (Enablement)

7. Claims 28-35 and 38-40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Additionally, (regarding the recitation of variants and fragments in the claims) at page 17 of the response of 02 February 2005, Applicant states that claims 28-32 are amended to recite a functional limitation that "the nucleic acid encoding the polypeptide is amplified in lung or colon tumors". Applicant asserts that since the claimed genus is now characterized by a combination of structural and functional features, any person of skill would know how to make and use the invention without undue experimentation based on the general knowledge in the art at the time the invention was made. Applicant cites *In re Certain Limited-charge cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), aff'. sub nom., *Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Circ. 1985) to emphasize the fact that experimentation may be complex does not necessarily make it undue.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, as discussed in the previous Office Action, certain positions in the polypeptide sequence are critical to the protein's structure/function relationship, e.g., such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the DNA and protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. A large quantity of experimentation would be required by the skilled artisan to generate the infinite number of derivatives recited in the claims and screen the same for activity. As was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving

predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). Furthermore, recitation of the phrase "the nucleic acid encoding the polypeptide is amplified in lung or colon tumors" in the claims is not adequate to describe the PRO1759 polypeptide or all possible variants that have at least 80%, 85%, 90%, 95%, and 99% homology to the PRO1759 polypeptide, since there was no reduction to practice to support the amended claims.

Additionally, it is noted that the fact pattern of the case cited by the Applicant (*In re Certain Limited-Charge Cell Culture Microcarriers*) and the fact pattern of the instant rejection are significantly different, and the court decision is not binding with regard to the instant rejection. For example, in *Certain Limited-Charge Cell Culture Microcarriers,* the main issue was patent validity and unfair competition. The patented claims are drawn to microcarrier beads for cell culture and a method of using the microcarriers for cell culture, not polynucleotide variants. Evidence has been cited on the record establishing that there is little guidance in the specification regarding which structural features are required in order to provide activity and that the prior art discloses the unpredictability of the effects of mutation on protein structure and function.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance

presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 U.S.C. § 112, first paragraph (written description)

9. Claims 28-35 and 38-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth for claims 28-40 at pg 11-13 of the previous Office Action (04 November 2004).

Applicant's arguments (02 February 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that Applicant contends that claims 28-32 are amended to recite a functional limitation that "the nucleic acid encoding the polypeptide is amplified in lung or colon tumors". Applicant argues that it is no longer true that the claims are drawn to a genus of polynucleotides defined by sequence identity alone. Applicant submits that this biological activity, coupled with a well-defined, and relatively high degree of sequence identity are believed to sufficiently define the claimed genus, such that one skilled in the art would readily recognize that the Applicant was in possession of the invention.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant has not described or shown possession of all polypeptides 80%, 85%, 90%, 95%, and 99% homologous to SEQ ID NO: 374, that still retain the function of SEQ ID NO: 374. Nor has Applicant described a representative number of species that have 80%, 85%, 90%, 95%, and 99% homology to SEQ ID NO: 374, such that it is clear that they were in possession of a genus of polypeptides functionally similar to SEQ ID NO: 374. As discussed in the previous Office Action (04 November 2004), even one skilled in the art could not envision the detailed chemical structure of all or a significant number of encompassed PRO1759 polypeptides, and therefore, would not know how to make or use them. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making. The claimed product itself is required. Recitation of the phrase "the nucleic acid encoding the polypeptide is amplified in lung or colon tumors" in the claims is not adequate to describe the PRO1759 polypeptide variants that have 80%, 85%, 90%, 95%, and 99% homology to the PRO1759 polypeptide, since there was no reduction to practice to support the amended claims. Applicants made no variant polypeptides, and as recited in the current Written Description Guidelines, Applicants must have invented the subject matter that is claimed and must be in "possession" of the claimed genus (Federal Register, 2001, Vol. 66, No. 4, pages 1099-1111, esp. page 1104, 3rd column).

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
18 April 2005

ELIZABETH KEMMERER
PRIMARY EXAMINER